REMARKS/ARGUMENTS

Claims 1-7 and 12-23 are pending in the Application. Claims 1-4 have been withdrawn from consideration by the Examiner as directed to an invention non-elected in response to a restriction requirement.

Independent Claim 5 and dependent Claims 13, 14, 16, 17, and 23 are currently amended. Claim 5 is currently amended to delete "and incorporating the powder into a water-soluble matrix of at least one pharmaceutically acceptable excipient" at the end and add the word "and" between the two "wherein" clauses. The claim is directed to the powder itself which is not incorporated into a water soluble matrix. Support therefore is found in the Specification at page 5, line 25, to page 6, line 9; page 6, line 24, to page 7, line 7; and original Claim 5. Claim 16 is amended to recite "from 1 to less than 3% by weight, based on the copolymer, of an emulsifier having an HLB of 14 or more" so not to exceed the "less than 3%" upper limit thereof in independent Claim 5. Support therefore is found in the Specification at page 10, lines 23-26. The amendments to Claims 13, 14, and 17 are editorial in nature. Claim 23 has been amended to more properly depend from the pharmaceutical composition of dependent Claim 19 which includes "at least one pharmaceutically acceptable excipient".

No new matter is added.

Attached hereto is the Declaration Under 37 CFR § 1.132 of Dr. Kathrin Nollenberger, dated January 25, 2010. The declaration is submitted in response to the Examiner's statement on page 11 of the Office Action dated June 5, 2009 (OA):

> Applicants argue that the superior bioavailability compared to the spray dried products such as those of Kajiyama results from the transfer of the active ingredient to a stadium of a solid solution during the melt process which produces the products of the invention.
>
> This is not persuasive because Applicant has not provided comparative evidence to show that the product produced by a melt process is superior to products prepared by a spray drying process. The instant specification also does not provide

comparisons between products produced by the two different processes. Moreover, instant claims are directed to a product and the limitations of the product are rendered obvious by the teachings of Kajiyama.

Rejections of Claims 5-7, 12-15, and 18-23 under 35 U.S.C. 103 over Kajiyama

Claims 5-7, 12-15, and 18-23 were rejected under 35 U.S.C. 103 over Kajiyama (U.S. Patent 5,545,492 [sic, 6,656,492], issued December 2, 2003)(OA, pp. 2-8, ¶ 5). In light of the evidence (A) in Applicant's Specification reporting bitter taste masking results for (1) claimed powders with and comparative powders without an anionic active pharmaceutical ingredient, and (2) claimed powders with and comparative powders without 5 to 50% by weight of a C_{12} to C_{22} carboxylic acid; and (B) in the attached Declaration Under 37 CFR § 1.132 of Dr. Kathrin Nollenberger, dated January 25, 2010, declaring that the claimed powders can be produced by Applicant's melt processing procedure and that the claimed powders cannot be produced by Kayiyama's spray drying procedure, the weight of the evidence of record favors patentability and the Examiner's rejections should be withdrawn.

1. The claimed invention

The Examiner concludes that Applicant's claims are directed to a powder with an average particle size of 200 μm or less which, when placed in the mouth, immediately disintegrates to release its active ingredient (OA, p. 2). The powder is produced by vigorously mixing (a) an anionic active pharmaceutical ingredient, (b) a copolymer consisting of free-radical polymerized C_1 to C_4 esters of acrylic or methacrylic acid and (meth)acrylate monomers which have functional tertiary amino groups, and (c) 5 to 50% by weight, based on (b), of a C_{12} to C_{22} carboxylic acid, in a melt, solidifying the mixture, and grinding the mixture to an active ingredient-containing powder with an average particle size of 200 μm or less (OA, pp. 2-3, bridging ¶). The powder produced by the process recited in the claim has an average particle size of 200 μm or less and comprises (a) an anionic active pharmaceutical ingredient, (b) a copolymer consisting of free-radical polymerized C_1 to C_4 esters of acrylic

or methacrylic acid and (meth)acrylate monomers which have functional tertiary amino groups, (c) 5 to 50% by weight, based on (b), of a C_{12} to C_{22} carboxylic acid, and (d) less than 3% by weight, based on the copolymer of an emulsifier having an HLB of at least 14 (OA, p. 2).

2. Kajiyama's powder

Kajiyama teaches a quick disintegrating tablet in the buccal cavity comprising bitter tasting drug-containing particles having a mean particle size of 50-250 μm, preferably 50-150 μm (Kajiyama, col. 1, ll. 14-18). Kajiyama's drug-containing particles are "obtained by spray drying" and consist of (1) a bitter tasting drug and (2) a pharmaceutical preparation carrier (Kajiyama, col. 1, ll. 19-22).

A. Kajiyama's bitter tasting drug

Kajiyama's bitter tasting drug may be any bitter tasting drug with no special restrictions as long as it is pharmaceutically active (Kajiyama, col. 6, ll. 38-41). While Kajiyama provides a long list of suitable bitter tasting drugs for use in its particles, including anionic ibuprofen (Kajiyama, col. 7, l. 18), it is evident from Kajiyama's list of bitter tasting drugs that Kajiyama's choice and selection of bitter tasting drugs is unlimited, and no bitter tasting drug employed in Kajiyama's examples is an anionic active drug (Kajiyama, col. 6, l. 38, to col. 7, l. 19; Examples 1-3 and 5 (famotidine); Example 4 (acetaminophen); Example 6 (ambroxol hydrochloride).

B. Kajiyama's pharmaceutical preparation carrier

Kajiyama's pharmaceutical preparation carrier also has no special restrictions "as long as it is pharmaceutically acceptable and alleviates the bitter taste of the drug, or improves fluidity of the drug, when spray dried with the drug" (Kajiyama, col. 8, ll. 5-11; emphasis added). Kajiyama's pharmaceutical preparation carrier includes "water insoluble polymers, gastrosoluble polymers, enterosoluble polymers, and wax-like substances, etc." (Kajiyama,

col. 8, ll. 11-14). Examples of water insoluble polymers suitable for use as Kajiyama's pharmaceutical preparation carrier are water-insoluble cellulose ethers and water-insoluble acrylic copolymers such as ethyl acrylate-methyl methacrylate-trimethyl ammonium chloride ethyl methacrylate copolymer, e.g., Eudragit® RS (Kajiyama, col. 8, ll. 13-22). Examples of gastrosoluble polymers suitable for use as Kajiyama's pharmaceutical preparation carrier are polyvinyl acetal diethyl aminoacetate and gastrosoluble acrylic copolymers such as methyl methacrylate-butyl methacrylate-dimethyl aminoethyl methacrylate copolymer, e.g., Eudragit® E (Kajiyama, col. 8, ll. 23-27). Examples of enterosoluble polymers suitable for use as Kajiyama's pharmaceutical preparation carrier are enterosoluble cellulose derivatives and enterosoluble acrylic acid copolymers, e.g., Eudragit® L (Kajiyama, col. 8, ll. 27-36). Examples of wax-like substances suitable for use as Kajiyama's pharmaceutical preparation carrier are solid fat and oils; higher fatty acids such as stearic acid, lauric acid, myristic acid, palmitic acid, etc.; and higher alcohols (Kajiyama, col. 8, ll. 36-41). Kajiyama prefers to use water-insoluble polymers as the pharmaceutical preparation carrier (Kajiyama, col. 8, ll. 41-48).

Kajiyama does not teach or reasonably suggest that mixtures of a water insoluble polymer or a gastrosoluble polymer or a enterosoluble polymer or a wax-like substance with any of the other particular functional kind of water insoluble or soluble polymer or wax-like substance should or may be used as the pharmaceutical preparation carrier for any reason. Again, Kajiyama states, "There are no special restrictions to the pharmaceutical preparation carrier used in the present invention as long as it is pharmaceutically acceptable and alleviates the bitter taste of the drug, or improves fluidity of the drug, when spray dried with the drug" (Kajiyama, col. 8, ll. 5-11; emphasis added).

C. Kajiyama's particles are "obtained by spray drying"

Kajiyama describes drug-containing particles "consisting of a bitter tasting drug . . . and a pharmaceutical preparation carrier and obtained by spray drying" (Kajiyama, col. 1, ll. 19-22; emphasis added). Kajiyama's prepares its drug-containing particles by "(a) the process whereby a bitter tasting drug . . . and a pharmaceutical preparation carrier are dissolved and suspended to approximately 30-approximately 70 w/w % in terms of solid concentration in a solvent that is pharmaceutically acceptable to prepare the suspension for spray drying, (b) the process whereby the suspension obtained process (a) is spray dried using a rotating disk-type spray drier . . . and (c) the process whereby the drug-containing particles obtained by process (b) and a saccharide are mixed and this mixture is molded" (Kajiyama, col. 1, ll. 24-39; col. 5, ll. 5-21; emphasis added). Kajiyama teaches (Kajiyama, col. 7, l. 65, to col. 8, l. 4):

> The term "obtained by spray drying" in the present Specification means the state of the drug alone or the drug together with a pharmaceutically acceptable carrier dissolved in a solvent that is pharmaceutically acceptable, or suspended with the drug or part or all of the carrier dispersed in a solvent and this solution or suspension being sprayed and dried.

Thus, the invention Kajiyama discloses and claims is a quick disintegrating tablet in buccal cavity comprising drug-containing particles including a bitter tasting drug and a pharmaceutical preparation carrier which are "obtained by spray drying" (Kajiyama, col. 1, ll. 19-22; and cols. 19-20, Claim 1). Kajiyama instructs (Kajiyama, col. 10, ll. 20-23; emphasis added), "The drug-containing particles obtained by spray drying of the present invention are made into a pharmaceutical preparation in the form of a quick disintegrating tablet in buccal cavity."

It is evident from the evidence of record, including the teaching in Kajiyama's disclosure as a whole, Applicant's Comparative Example 6 (active ingredient caffeine not according to the invention), Comparative Examples 8 and 9 (active ingredient paracetamol

not according to the invention), Comparative Example 7 (without stearic acid), Comparative Example 12 (C_{12} alcohol compound instead of stearic acid), and the attached Declaration Under 37 CFR § 1.132 of Dr. Kathrin Nollenberger, dated January 25, 2010, that Kajiyama does not disclose or reasonably suggest any powder defined by Applicant's currently amended claims.

First, Applicant's claimed powder comprises an anionic active pharmaceutical ingredient. Examples 2 and 5 on pages 17-19 of the Specification and Comparative Examples 6, 8, and 9 on pages 19-20 of the Specification show that melt processed products comprising 1 mol of Eudragit® E PO, 0.5 mol of stearic acid, and either 1 mol, 1.58 mol, or 2.03 mol of a drug which is not anionic do not mask the bitter taste of the drug after 10s in the mouth whereas melt processed products comprising 1 mol of Eudragit® E PO, 0.5 mol of stearic acid, and either 0.66 mol or 1 mol of an anionic drug masks the bitter taste of the drug for at least 1 minute. Based on Kajiyama's disclosure, persons having ordinary skill in the art reasonably would have expected no differences in the bitter taste masking properties of the compositions depending on the type of drug. The evidence shows that the choice of an anionic drug in the claimed particles not only produces immediate disintegration and release of the drug but unexpectedly masks the bitter taste of the anionic drug in the mouth for at least one minute.

Second, Applicant's claimed powder comprises 5 to 50% by weight of a C_{12} to C_{22} carboxylic acid. Examples 1-4 on pages 17-19 of the Specification and Comparative Example 7 on pages 19-20 of the Specification show that melt processed products comprising 1 mol of Eudragit® E PO, ~0.66 mol of ibuprofen, 0.18 mol talc and no C_{12} to C_{22} carboxylic acid do not mask the bitter taste of the drug after 10s in the mouth whereas melt processed products comprising 1 mol of Eudragit® E PO, 0.33 to 1 mol of stearic acid, and 0.66 mol of ibuprofen mask the bitter taste of the drug for at least one minute. Based on Kajiyama's

disclosure, persons having ordinary skill in the art reasonably would have expected no differences in the bitter taste masking properties of the compositions depending on the inclusion of a C_{12} to C_{22} carboxylic acid in the particles. The evidence shows that the inclusion of a C_{12} to C_{22} carboxylic acid in the claimed particles not only produces immediate disintegration and release of the drug but unexpectedly masks the bitter taste of the anionic drug in the mouth for at least one minute.

Third, Applicant's claimed powder comprises 5 to 50% by weight of a C_{12} to C_{22} carboxylic acid. Examples 4 on pages 18-19 of the Specification and Comparative Example 12 on pages 21-22 of the Specification show that melt processed products comprising 1 mol of Eudragit® E PO, ~0.66-0.77 mol of ibuprofen, and 0.34 of a C_{12} alcohol do not mask the bitter taste of the drug after 20s in the mouth whereas melt processed products comprising 1 mol of Eudragit® E PO, 0.66 mol of ibuprofen, and 0.33 of C_{12} carboxylic acid masks the bitter taste of the drug for at least one minute. Based on Kajiyama's disclosure, persons having ordinary skill in the art reasonably would have expected no differences in the bitter taste masking properties of the compositions depending on the inclusion of either a C_{12} alcohol or a C_{12} carboxylic acid in the particles. However, the evidence shows that the inclusion of a C_{12} carboxylic acid in the claimed particles not only produces immediate disintegration and release of the drug but unexpectedly masks the bitter taste of the anionic drug in the mouth for at least one minute.

Finally, Kajiyama's particles are "obtained by spray drying" (Kajiyama, Abstract; col. 10, ll. 21-23; cols. 19-20, Claims 1 and 13). Kajiyama does not disclose or suggest the melt processing steps by which the powders of Applicant's Claims 5-7 and 12-18 or the powder in the compositions of Applicant's dependent Claims 19-23 are made. Moreover, if the evidence of record shows that the pertinent particles generally disclosed or reasonably suggested by Kajiyama cannot be "obtained by spray drying" as Kajiyama requires and/or

Kajiyama would not have enabled persons having ordinary skill in the art to make and use those particles by any other process but spray drying without undue experimentation and with reasonable expectation of success, then the particles made by Applicant's claimed melt processing procedure are not disclosed by Kajiyama and reasonably would not have been obvious to a person having ordinary skill in the art in view of Kajiyama's teaching as a matter of law.

The Declaration Under 37 CFR § 1.132 of Dr. Kathrin Nollenberger, dated January 25, 2010, states that particles comprising Eudragit® E PO, stearic acid, and ibuprofen (an anionic active ingredient) were obtained by Applicant's melt processing procedure. However, the declaration explains that particles comprising Eudragit® E PO, stearic acid, and ibuprofen (an anionic active ingredient) could not be obtained by spray drying in accordance with Kajiyama's disclosure and cannot be obtained without undue experimentation. Accordingly, Applicant's claimed powder made by the melt processing procedure required in all of Applicant's claims, and Applicant's claimed compositions comprising the claimed powder made by the melt processing procedure required in all Applicant's claims, are not enabled, are not described, and are not reasonably suggested by Kajiyama's disclosure.

For a claimed composition of matter to be obvious under 35 U.S.C. § 103 in view of prior art, the prior art must place the composition in the possession of the public. *In re Donohue*, 766 F.2d 531, 534 (Fed. Cir. 1985). To place the composition in the possession of the public, the prior art must enable one skilled in the art to make and use the subject matter the applicant claims. *In re Hoeksema*, 399 F.2d 269, 274 (CCPA 1968). Therefore, to make a case for unpatentability under 35 U.S.C. § 102 or § 103, the applied prior art must enable persons skilled in the art to make and use the invention without undue experimentation. *Impax Labs., Inc. v. Aventis Pharm. Inc.*, 545 F.3d 1312, 1314 (Fed. Cir. 2008). If undue experimentation is required to make and use the subject matter Applicant claims, the prior art

does not enable persons skilled in the art to make and use that subject matter. *In re Vaeck*, 947 F.2d 488, 495 (Fed. Cir. 1991). Without an enabling prior art disclosure, there is no reasonable basis for a conclusion of obviousness.

Kajiyama teaches, and enables one skilled in the art to make and use, a quick disintegrating tablet comprising particles having a mean diameter of less than 150 μm "obtained by spray drying". The particles comprise a bitter tasting drug and a pharmaceutical preparation carrier, but they must be obtainable by spray drying without undue experimentation. The evidence of record shows that the powder Applicant claims comprising (a) an anionic active pharmaceutical ingredient, (b) a copolymer which consists of free-radical polymerized C_1 to C_4 esters of acrylic or methacrylic acid and further (meth)acrylate monomers whichhave functional tertiary amino groups, (c) 5 to 50% by weight, based on (b), of a C_{12} to C_{22} carboxylic acid, and (d) less than 3% by weight, based on the copolymer, of an emulsifier having an HLB of at least 14, could not be obtained by spray drying and cannot be obtained without undue experimentation. Kajiyama does not disclose or reasonably suggest any method other than spray drying to make and use particles comprising a bitter tasting drug and a pharmaceutical preparation carrier which not only quickly disintegrates and releases the bitter tasting drug but also unexpectedly masks the bitter taste of the drug in the mouth for any period of time. Moreover, the evidence shows that Applicant unexpectedly achieved bitter taste masking of at least one minute with powder made by melt processing.

The evidence of record shows that the claimed powder which immediately disintegrates in the mouth and masks the bitter taste of the drug was made by melt processing (a) an anionic drug, a copolymer which consists of free-radical polymerized C_1 to C_4 esters of acrylic or methacrylic acid and further (meth)acrylate monomers which have functional tertiary amino groups, and (c) 5 to 50% by weight, based on (b), of a C_{12} to C_{22} carboxylic acid, and (d) less than 3% by weight, based on the copolymer, of an emulsifier having an

HLB of at least 14 but could not be made by spray drying. To the contrary, Kajiyama would have taught persons having ordinary skill in the art that there are no restrictions on the kind of bitter tasting drug or the kind of pharmaceutical preparation carrier except that the combination "alleviates the bitter taste of the drug, or improves fluidity of the drug, when spray dried with the drug" (Kajiyama, col. 8, ll. 5-11; col. 6, ll. 38-41).

The evidence of record shows, contrary to Kajiyama's teaching, that the kind of drug is critical for success, the kinds, combinations, and amounts of pharmaceutical preparation carriers are critical for success, the kind and amount of emulsifiers are critical for success, and the use of melt processing is critical for successfully preparing a powder having an average particle size of less than 200 μm and containing a bitter tasting drug, which powder, when placed in the mouth, not only immediately disintegrates and releases the drug but also masks the bitter taste of the drug in the mouth for at least one minute.

In light of Kajiyama's disclosure, undue experimentation would have been required to make and use the powder and compositions Applicant currently claims with reasonable expectation of success. The evidence of record shows that the Examiner erred in concluding that the subject matter Applicant claims would have been enabled by, and obvious to a person having ordinary skill in the art in view of, the teaching of Kajiyama. Kajiyama neither suggests the problems one skilled in the art would face making and using a quick release powder which effectively masks the bitter taste of the drug in the mouth nor would not have suggested any solutions to those problems without undue experimentation.

Finally, nothing in Kajiyama's disclosure would have led persons having ordinary skill in the art to understand of even believe that the specific combination of an anionic active pharmaceutical ingredient (a), gastrosoluble copolymer (b), 5 to 50% of a higher fatty acid (c), less than 3% by weight of an emulsifier having a HLB of at least 14, and melt processing is essential to making and using the superior powders and compositions Applicant claims.

With all due respect, the subject matter Applicant now claims is patentable over the applied prior art.

Rejections of Claims 16-17 under 35 U.S.C. 103 over Kajiyama in view of Smith

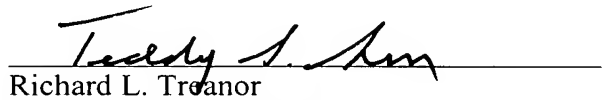
Claims 16-17 were rejected under 35 U.S.C. §103(a) as unpatentable over Kajiyama in view of Smith (U.S. Patent No. 6,194,00, issued February 27, 2001). The evidence of record shows that Kajiyama does not reasonably suggest the claimed powder and compositions with the requisite enabling disclosure and reasonable expectation of success.

Smith is relied upon for its teaching that pharmaceutical powder suitable for immediate release may contain sodium lauryl sulphate as an emulsifier having an HLB of at least 14. However, not only does Smith not remedy any of Kajiyama's deficiencies, but the Examiner has not explained why Smith's disclosure of sodium lauryl sulphate for use in its immediate release particles would have led persons having ordinary skill in the art to add and critically limit the amount of the additive in Applicant's claimed powder to less than 3% by weight. The Examiner has the initial burden of proof to establish a factual basis for the conclusion of prima facie obviousness. *In re Fine*, 837 F.2d 1071, 1074 (Fed. Cir. 1988); *In re Piasecki*, 745 F.2d 1468, 1472 (Fed. Cir. 1984). Left unexplained, this rejection should be withdrawn.

For the reasons stated herein, the claimed subject matter is patentable over the applied prior art and in condition for allowance. Early Notice of Allowance is respectfully requested.

Respectfully submitted,

OBLON, SPIVAK, McCLELLAND,
MAIER & NEUSTADT, P.C.
Norman F. Oblon



Richard L. Treanor
Registration No. 36,379

Teddy S. Gron
Registration No. 63,062

Customer Number
22850

Tel: (703) 413-3000
Fax: (703) 413-2220
(OSMMN 08/07)